Final Progress Report for Research Projects Funded by Health Research Grants

Instructions: Please complete all of the items as instructed. Do not delete instructions. Do not leave any items blank; responses must be provided for all items. If your response to an item is "None", please specify "None" as your response. "Not applicable" is not an acceptable response for any of the items. There is no limit to the length of your response to any question. Responses should be single-spaced, no smaller than 12-point type. The report **must be completed using MS Word**. Submitted reports must be Word documents; they should not be converted to pdf format. Questions? Contact Health Research Program staff at 717-783-2548.

1. **Grantee Institution:** Allegheny-Singer Research Institute

2. **Reporting Period (start and end date of grant award period):** January 1, 2012 – December 31, 2013

3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** Rebecca Pfeifer, Manager, Grants and Contracts

4. **Grant Contact Person's Telephone Number:** 412-359-3137

5. **Grant SAP Number:** 4100057651

6. **Project Number and Title of Research Project:** Utility of Cognitive Testing in the Detection of Residual Impairment Following Concussion

7. **Start and End Date of Research Project:** January 1, 2012 – December 31, 2013

8. **Name of Principal Investigator for the Research Project:** Kevin M. Kelly, M.D., Ph.D.

9. **Research Project Expenses**. $98,254.00

   9(A) Please provide the total amount of health research grant funds spent on this project for the entire duration of the grant, including indirect costs and any interest earned that was spent:

   $ 98,666.30

   9(B) Provide the last names (include first initial if multiple individuals with the same last name are listed) of **all** persons who worked on this research project and were supported with health research funds. Include position titles (Principal Investigator, Graduate Assistant, Post-doctoral Fellow, etc.), percent of effort on project and total health research funds expended for the position. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name, First Name	Position Title	% of Effort on Project	Cost
Kelly, Kevin M.	Principal Investigator	2.6%	$13,483.08
Hentosz, Teresa	Research Assistant	34%	$18,620.68
Miller, Eric	Research Assistant	100%	$27,470.69
Ulisse, Krista	Summer Intern	100%	$0
King, Justin	Summer Intern	100%	$0

9(C) Provide the names of **all** persons who worked on this research project, but who *were not* supported with health research funds. Include position titles (Research Assistant, Administrative Assistant, etc.) and percent of effort on project. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name, First Name	Position Title	% of Effort on Project
Schramke, Carol	Investigator	5%
Snell, Edward	Investigator	5%
Bauer, Missy	Research Assistant	5%

9(D) Provide a list of **all** scientific equipment purchased as part of this research grant, a short description of the value (benefit) derived by the institution from this equipment, and the cost of the equipment.

Type of Scientific Equipment	Value Derived	Cost
N/A		

10. Co-funding of Research Project during Health Research Grant Award Period. Did this research project receive funding from any other source during the project period when it was supported by the health research grant?

Yes_____ No__X_____

If yes, please indicate the source and amount of other funds:

11. Leveraging of Additional Funds

11(A) As a result of the health research funds provided for this research project, were you able to apply for and/or obtain funding from other sources to continue or expand the research?

Yes__X_____ No_____

If yes, please list the applications submitted (column A), the funding agency (National Institutes of Health—NIH, or other source in column B), the month and year when the application was submitted (column C), and the amount of funds requested (column D). If you have received a notice that the grant will be funded, please indicate the amount of funds to be awarded (column E). If the grant was not funded, insert "not funded" in column E.

Do not include funding from your own institution or from CURE (tobacco settlement funds). Do not include grants submitted prior to the start date of the grant as shown in Question 2. If you list grants submitted within 1-6 months of the start date of this grant, add a statement below the table indicating how the data/results from this project were used to secure that grant.

A. Title of research project on grant application	B. Funding agency (check those that apply)	C. Month and Year Submitted	D. Amount of funds requested:	E. Amount of funds to be awarded:
Longitudinal Study of mTBI as Measured by NKI Concussion Score	☐NIH X Other federal (specify: Dept. of Defense) ☐ Nonfederal source (specify: _____)	2-2012	$190,671	$0
*Rapid Innovation Fund – NKI Concussion Score	☐NIH X Other federal (specify: Dept. of Defense) ☐ Nonfederal source (specify: _____)	3-2012	$215,451	$215,451
Oculomotor and Vestibular Testing Following Sports-Related mTBI	X NIH ☐ Other federal (specify:_____ _____) ☐ Nonfederal source (specify:	5-2013	$409,928	$0

	_____)			

*Although data/results from this research project were not available at the time of submission of "Rapid Innovation Fund – NKI Concussion Score" to the Department of Defense, our institution's experience with neurocognitive testing (ImPACT) had strongly suggested significant limitations with its use for the diagnosis and management of concussion/mild traumatic brain injury (mTBI). These clinical considerations fostered exploration and development of improved diagnostic technologies for mTBI and promoted newly established collaborations with industry partners (NeuroKinetics, Inc., NKI) to advance the potential use of oculomotor and vestibular testing in soldiers who had experienced blast or blunt mTBI, the focus of the successful submission of "Rapid Innovation Fund – NKI Concussion Score."

11(B) Are you planning to apply for additional funding in the future to continue or expand the research?

Yes___X_____ No_____

If yes, please describe your plans:

In collaboration with the Allegheny Health Network (AHN) Sports Medicine Program and NKI, I became the PI of an unfunded clinical pilot study between AHN and NKI utilizing NKI's oculomotor and vestibular I-Portal testing system, for which we have completed enrollment and testing - all post-injury with no baseline testing done - of 50 middle school and high school student athletes who sustained sports-related concussions. Many of these student athletes (n=20; 40%) underwent multiple sequential evaluations with the NKI I-Portal system administered over variable periods of time during their recovery period. The data derived from these studies are currently being analyzed, including comparison of the results of the protocol's concurrent testing performed with ImPACT and the Allegheny General Hospital Standardized Concussion Assessment Tool (AGHSCAT). Following completion of this analysis, we plan to submit an improved R21 application to NINDS to more comprehensively assess the utility of this technology for sports-related mTBI in high school student athletes (please see below).

12. Future of Research Project. What are the future plans for this research project?

In order to standardize and optimize evaluation with the NKI I-Portal system, we plan to evaluate student athletes at preseason baseline, within an hour, or even minutes, of a sports-related mTBI, within 72 h, and at 1-week, 2-week, and 1-month time points post-injury; the majority of the testing will be school-based and performed by certified athletic trainers. This study will allow us to validate the oculomotor and vestibular metrics that have heretofore been preliminarily correlated with the diagnosis of mTBI, and to potentially expand the technology's use to determine the correlation – and potential utility - of serial testing results with clinical metrics of recovery from the mTBI.

13. New Investigator Training and Development. Did students participate in project supported internships or graduate or post-graduate training for at least one semester or one summer?

Yes___X_____ No_____

If yes, how many students? Please specify in the tables below:

	Undergraduate	Masters	Pre-doc	Post-doc
Male	1			
Female	1			
Unknown				
Total	**2**			

	Undergraduate	Masters	Pre-doc	Post-doc
Hispanic	0	0	0	0
Non-Hispanic	0	0	0	0
Unknown	2	0	0	0
Total	**2**	**0**	**0**	**0**

	Undergraduate	Masters	Pre-doc	Post-doc
White	2	0	0	0
Black	0	0	0	0
Asian	0	0	0	0
Other	0	0	0	0
Unknown	0	0	0	0
Total	**2**	**0**	**0**	**0**

14. Recruitment of Out-of–State Researchers. Did you bring researchers into Pennsylvania to carry out this research project?

Yes_____ No__X_____

If yes, please list the name and degree of each researcher and his/her previous affiliation:

15. Impact on Research Capacity and Quality. Did the health research project enhance the quality and/or capacity of research at your institution?

Yes___X_____ No_____

If yes, describe how improvements in infrastructure, the addition of new investigators, and other resources have led to more and better research.

The health research project enhanced the quality and capacity of research at our institution by enabling a first-time, cross-departmental collaboration of researchers from the Department of Neurology with researchers from the Department of Orthopedic Surgery's Sports Medicine Program. Infrastructure was enhanced by the development of a model patient registry that could be used for all subsequent testing for suspected or known mTBI. The health research project also established in-depth, retrospective clinical investigatory best practices for three research assistants who had limited or no clinical research experience, and two summer interns who had no research experience beyond undergraduate laboratory courses.

16. Collaboration, business and community involvement.

16(A) Did the health research funds lead to collaboration with research partners outside of your institution (e.g., entire university, entire hospital system)?

Yes___X_____ No_____

If yes, please describe the collaborations:

The health research funds led to a very successful collaboration with an industry partner, NeuroKinetics, Inc., with whom we have completed a large pilot study of their I-Portal's oculomotor and vestibular testing system in 50 student athletes aged 13-18 that had sustained a sports-related concussion. The collaboration also resulted in a successful application to the Department of Defense's Rapid Innovation Fund Contract 12097010 to study the utility of the I-Portal technology in soldiers that experienced either blast or blunt mTBI.

16(B) Did the research project result in commercial development of any research products?

Yes_____ No___X_____

If yes, please describe commercial development activities that resulted from the research project:

16(C) Did the research lead to new involvement with the community?

Yes_____ No___X_____

If yes, please describe involvement with community groups that resulted from the research project:

The research led to one community presentation: 1) "Evaluation Standards for Concussion Management" to parents and athletic trainers of middle school and high

school student athletes, Guidelines for Initial Concussion Management, Pennsylvania State University – New Kensington Campus, March, 2013.

17. Progress in Achieving Research Goals, Objectives and Aims.

List the project goals, objectives and specific aims (as contained in the grant agreement). Summarize the progress made in achieving these goals, objectives and aims for the period that the project was funded (i.e., from project start date through end date). Indicate whether or not each goal/objective/aim was achieved; if something was not achieved, note the reasons why. Describe the methods used. If changes were made to the research goals/objectives/aims, methods, design or timeline since the original grant application was submitted, please describe the changes. Provide detailed results of the project. Include evidence of the data that was generated and analyzed, and provide tables, graphs, and figures of the data. List published abstracts, poster presentations and scientific meeting presentations at the end of the summary of progress; peer-reviewed publications should be listed under item 20.

This response should be a DETAILED report of the methods and findings. It is not sufficient to state that the work was completed. Insufficient information may result in an unfavorable performance review, which may jeopardize future funding. If research findings are pending publication you must still include enough detail for the expert peer reviewers to evaluate the progress during the course of the project.

Health research grants funded under the Tobacco Settlement Act will be evaluated via a performance review by an expert panel of researchers and clinicians who will assess project work using this Final Progress Report, all project Annual Reports and the project's strategic plan. After the final performance review of each project is complete, approximately 12-16 months after the end of the grant, this Final Progress Report, as well as the Final Performance Review Report containing the comments of the expert review panel, and the grantee's written response to the Final Performance Review Report, will be posted on the CURE Web site.

There is no limit to the length of your response. Responses must be single-spaced below, no smaller than 12-point type. If you cut and paste text from a publication, be sure symbols print properly, e.g., the Greek symbol for alpha (α) and beta (ß) should not print as boxes (□) and include the appropriate citation(s). DO NOT DELETE THESE INSTRUCTIONS.

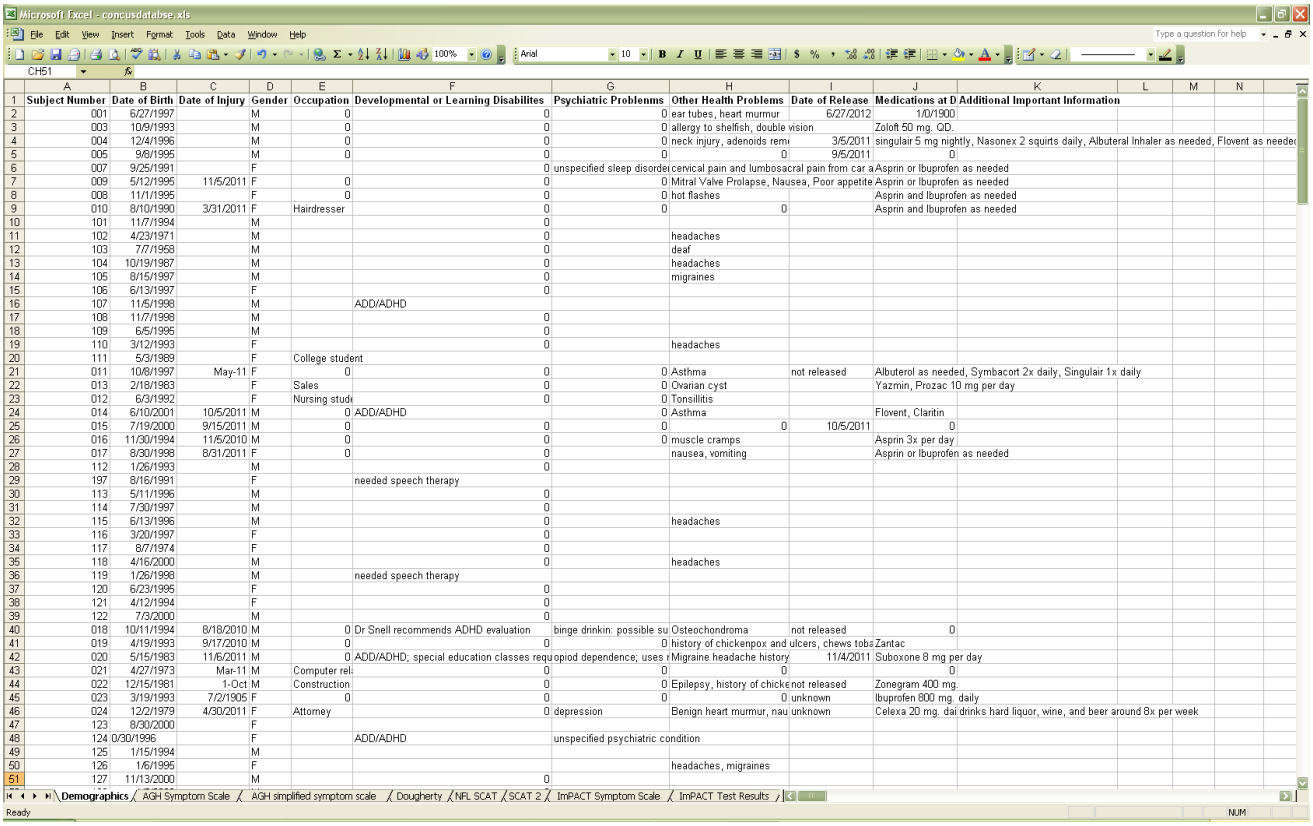
Project Title and Purpose

Utility of Cognitive Testing in the Detection of Residual Impairment Following Concussion – This project will evaluate data obtained in the clinical evaluation of individuals who have sustained a concussion. The purpose of this research is to: 1) ensure that clinical evaluations and the tools that we use to evaluate patients following concussions are sufficiently comprehensive to be sensitive to the sequelae of concussion; 2) make the best-informed decisions regarding returning to normal activities and minimizing the risk of re-injury and problems at school and work; and 3) reduce the likelihood that financial resources are used to obtain data that are redundant, not clinically useful, and unnecessarily increase health care costs.

Summary of Research Completed

A total of 284 charts from patients seen during a 2.5-year period - January 1, 2010 to June 30, 2012 - at Allegheny General Hospital's Sports Medicine Concussion Clinic were screened for the presence of a baseline and a post-injury ImPACT report. Each chart was de-identified when entering patient data into a comprehensive Excel spreadsheet on a password-protected hospital computer kept in a locked office area of Dr. Kelly's Neurology Research Laboratory. Subjects' names and other identifiers were kept separate from the database collection tool and linked using a numeric code. The database included:

1) Demographic data (age, gender, occupation, developmental or learning disabilities, psychiatric problems, other health problems, date of release, medicines at date of evaluation, other injuries). Please see below an example of demographic data entry into the Excel spreadsheet.



Microsoft Excel - concusdatabse.xls

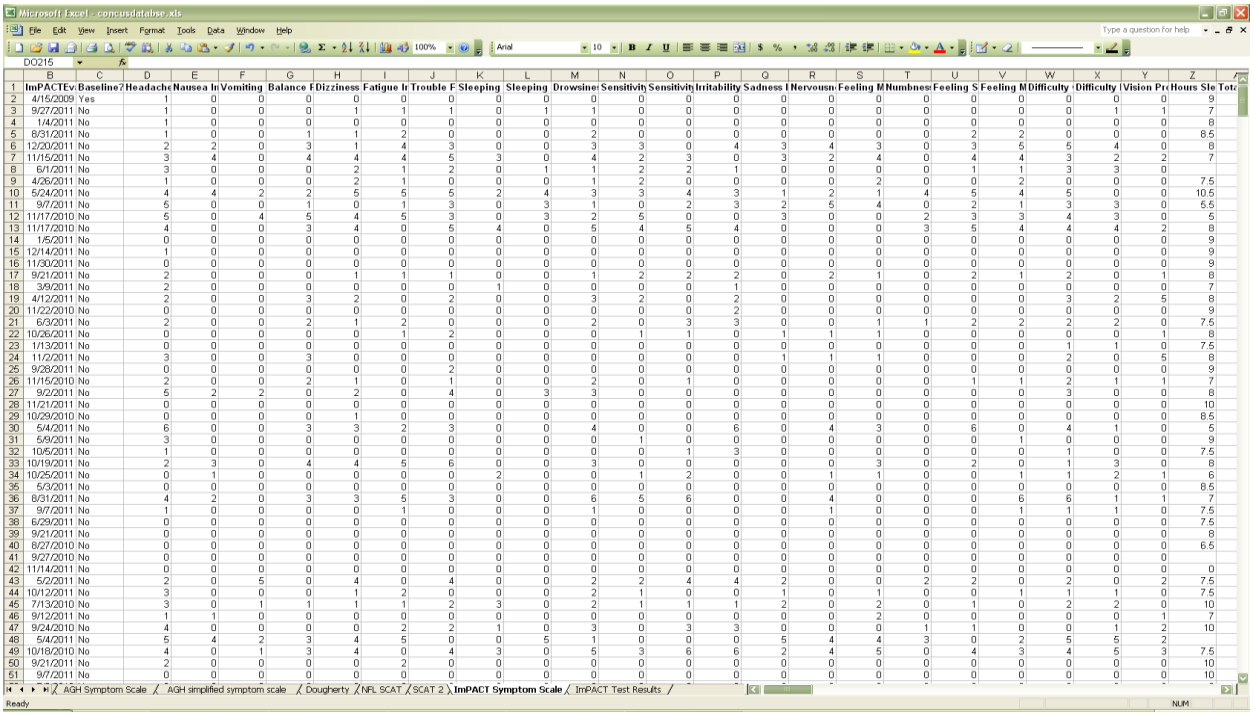
	Subject Number	Date of Birth	Date of Injury	Gender	Occupation	Developmental or Learning Disabilites	Psychiatric Problenms	Other Health Problems	Date of Release	Medications at D	Additional Important Information
2	001	6/27/1997		M	0	0	0	ear tubes, heart murmur	6/27/2012	1/0/1900	
3	003	10/9/1993		M	0	0	0	allergy to shelfish, double vision		Zoloft 50 mg. QD.	
4	004	12/4/1996		M	0	0	0	neck injury, adenoids rem	3/5/2011	singulair 5 mg nightly, Nasonex 2 squirts daily, Albuteral Inhaler as needed, Flovent as needed	
5	005	9/6/1995		M	0	0	0	0	9/5/2011	0	
6	007	9/25/1991		F		0	unspecified sleep disorder	cervical pain and lumbosacral pain from car a		Asprin or Ibuprofen as needed	
7	009	5/12/1995	11/5/2011	F	0	0	0	Mitral Valve Prolapse, Nausea, Poor appetite		Asprin or Ibuprofen as needed	
8	008	11/1/1995		F	0	0	0	hot flashes		Asprin and Ibuprofen as needed	
9	010	8/10/1990	3/31/2011	F	Hairdresser	0	0	0		Asprin and Ibuprofen as needed	
10	101	11/7/1994		M		0					
11	102	4/23/1971		M		0		headaches			
12	103	7/7/1958		M		0		deaf			
13	104	10/19/1987		M		0		headaches			
14	105	8/15/1997		M		0		migraines			
15	106	6/13/1997		F		0					
16	107	11/5/1998		M		ADD/ADHD					
17	108	11/7/1998		M		0					
18	109	6/5/1995		M		0					
19	110	3/12/1993		F		0		headaches			
20	111	5/3/1989		F	College student						
21	011	10/8/1997	May-11	F	0	0	0	Asthma	not released	Albuterol as needed, Symbacort 2x daily, Singulair 1x daily	
22	013	2/18/1983		F	Sales	0	0	Ovarian cyst		Yazmin, Prozac 10 mg per day	
23	012	6/3/1992		F	Nursing stud	0	0	Tonsillitis			
24	014	6/10/2001	10/5/2011	M	0	ADD/ADHD	0	Asthma		Flovent, Claritin	
25	015	7/19/2000	9/15/2011	M	0	0	0	0	10/5/2011	0	
26	016	11/30/1994	11/5/2010	M	0	0	0	muscle cramps		Asprin 3x per day	
27	017	8/30/1998	8/31/2011	F	0	0		nausea, vomiting		Asprin or Ibuprofen as needed	
28	112	1/26/1993		M		0					
29	197	8/16/1991		F		needed speech therapy					
30	113	5/11/1996		M		0					
31	114	7/30/1997		M		0					
32	115	6/13/1996		M		0		headaches			
33	116	3/20/1997		F		0					
34	117	8/7/1974		F		0					
35	118	4/16/2000		M		0		headaches			
36	119	1/26/1998		M		needed speech therapy					
37	120	6/23/1995		F		0					
38	121	4/12/1994		F		0					
39	122	7/3/2000		M		0					
40	018	10/11/1994	8/18/2010	M	0	Dr Snell recommends ADHD evaluation	binge drinkin: possible su	Osteochondroma	not released	0	
41	019	4/19/1993	9/17/2010	M	0	0	0	history of chickenpox and ulcers, chews tobs		Zantac	
42	020	5/15/1983	11/6/2011	M	0	ADD/ADHD; special education classes requ	opiod dependence; uses r	Migraine headache history	11/4/2011	Suboxone 8 mg per day	
43	021	4/27/1973	Mar-11	M	Computer rel	0	0	0		0	
44	022	12/15/1981	1-Oct	M	Construction	0	0	Epilepsy, history of chicke	not released	Zonegram 400 mg.	
45	023	3/19/1993	7/2/1905	F	0	0	0	0	unknown	Ibuprofen 800 mg. daily	
46	024	12/2/1979	4/30/2011	F	Attorney	0	depression	Benign heart murmur, nau	unknown	Celexa 20 mg. dai	drinks hard liquor, wine, and beer around 8x per week
47	123	8/30/2000		F							
48	124	0/30/1996		F		ADD/ADHD	unspecified psychiatric condition				
49	125	1/15/1994		M							
50	126	1/6/1995		F				headaches, migraines			
51	127	11/13/2000		M		0					

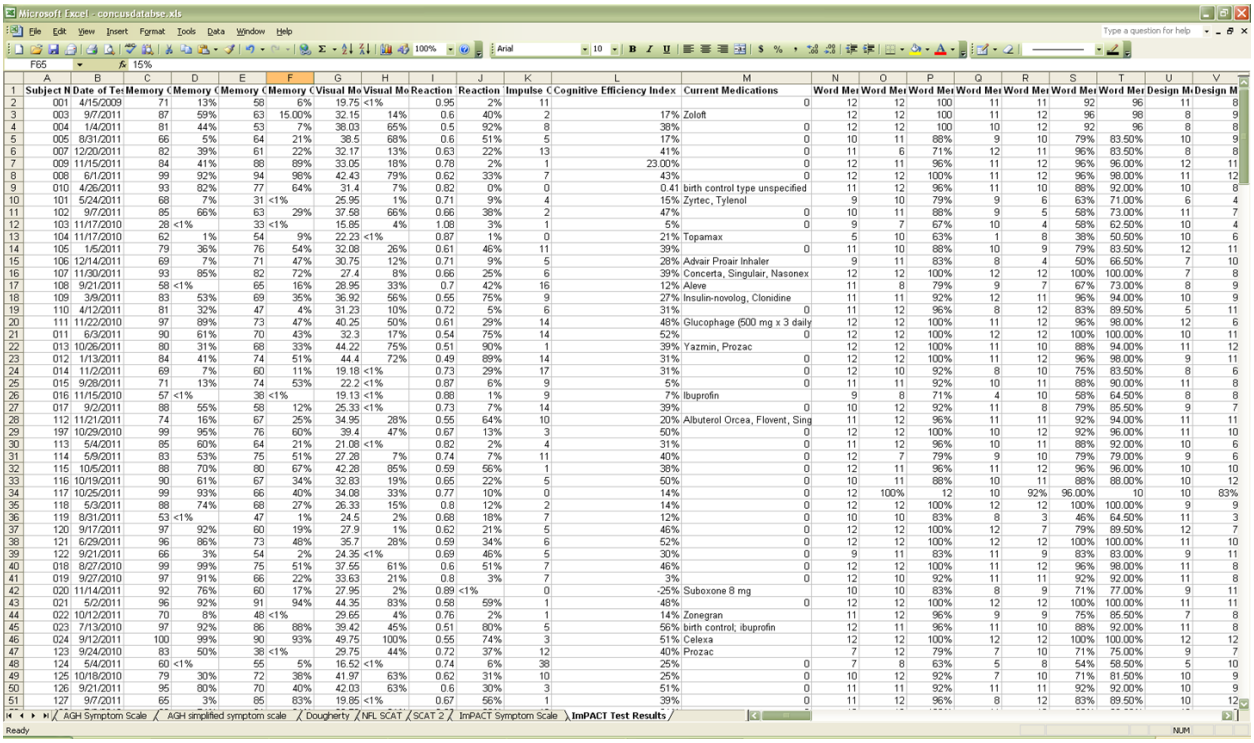
Demographics | AGH Symptom Scale | AGH simplified symptom scale | Dougherty | NFL SCAT | SCAT 2 | ImPACT Symptom Scale | ImPACT Test Results

Ready NUM

2) ImPACT data (date of testing, memory composite score, verbal composite score and percent, visual composite score and percent, visual motor speed score and percent, reaction time composite score and percent, cognitive efficiency index, current medications, word memory hits (immediate), word memory correct distractors (immediate), word memory learning percent correct, word memory hits (delay), word memory correct distractors (delay), word memory delayed memory percent correct, word memory total percent correct, design memory hits (immediate), design memory correct distractors (immediate), design memory learning percent correct, design memory hits (delay), design memory correct distractors (delay), design memory percent correct, design memory total percent correct, X's and O's Total Correct Memory, X's and

O's Total Correct (Interference), X's and O's average correct RT, X's and O's total incorrect interference, X's and O's average incorrect (interference), symbol matching total correct (visible), symbol matching average correct RT (visible), symbol matching total correct (hidden), symbol matching average correct RT (hidden), color match total correct, color match average correct RT, total correct, average correct RT, three letters total sequence correct, three letters total letters correct, three letters percent of total letters correct, three letters average time to 1st click, three letters average counted, three letters average counted correct). Please see below examples of ImPACT data entry into Excel spreadsheets for symptom severity and computer-based cognitive testing.





3) SCAT2/NFL SCAT data (date of assessment, working at date of testing, in school at date of testing, examiner, medications at date of testing, total symptom score, headache, pressure in head, neck pain, nausea or vomiting, dizziness, blurred vision, balance problems, sensitivity to light, sensitivity to noise, feeling slowed down, feeling like in a fog, don't feel right, difficulty concentrating, difficulty remembering, fatigue or low energy, confusion, drowsiness, trouble falling asleep, more emotional, irritability, sadness, nervousness or anxiety, loss of consciousness or unresponsiveness, duration, balance problems or unsteadiness, Glasgow coma scale score, best eye opening score, best verbal response score, best motor response score, Maddocks score, SAC score, orientation score, immediate memory score, concentration score, delayed recall score, balance examination score, double leg stance, single leg stance, tandem stance, coordination examination score, subtotal without SAC, total SCAT-2 score, clearance to return to play).

4) AGH Sports Medicine Patient Inventory form (evaluation date, date of injury, occupation, cause of injury, evidence of intracranial injury or fracture, evidence of forcible blow to head or neck, location of impact, loss of consciousness, seizures observed, retrograde amnesia, duration, anterograde amnesia, duration, pulled from activity, relative brain rest, hospital evaluation, CT scan, MRI, number of previous concussions, headache history, developmental history, psychiatric history, neurocognitive testing, orientation score, immediate memory, concentration score, months score, clock or object drawing, cranial nerves, coordination, BESS, delayed recall)

5) Symptoms evaluation (headache, nausea, vomiting, dizziness, blurred vision, balance problems, sensitivity to light or to noise, feeling slow, difficulty concentrating, remembering, fatigue or low energy, confusion, drowsiness, sleeping more or less, trouble falling asleep, more emotional, irritability, sadness, nervous or anxious).

6) Clinical evaluation (location of impact, loss of consciousness, pulled from activity, evidence of intracranial injury or fracture, evidence of forcible blow to head or neck, number of previous concussions, family history of headaches or migraines, imaging studies, clearance to return to play or school).

Specific Aim #1: Assess the frequency of initial pre-test ImPACT data being invalid.
This Aim was achieved. Each baseline ImPACT was reviewed for questionable validity using standardized measures provided by ImPACT. These measures examined sub-scale category scores individually and provided cutoff values for each of the 8 categories tested. Cutoff values are defined as scores falling below two standard deviations of the average score based on age and sex. Any score falling below these values is suggested, by ImPACT, to represent a possible invalid baseline test. Results from both valid and possibly invalid tests were compared with the first post-injury ImPACT test taken by each patient. Comparisons were made between percentile rankings in each of the 4 composite score categories. Differences in score were then analyzed to determine the number of possible patients that would have been misdiagnosed had no baseline information been present.

Seventy-two patients fit the described criteria for inclusion into the study. Of these 72 patients aged 11-18 years, 53 were males, 19 were females. Using the criteria set forth by ImPACT, 36 baseline examinations were found to have potential invalidity, while 36 were considered to be valid, i.e., possible invalid baseline studies represented 50% of the sample analyzed. Comparing possible invalid baseline and post-test scores in each of ImPACT's 4 composites categories revealed that following injury: 10 patients improved in verbal memory following injury; 11 patients improved in visual memory; 7 patients improved on visual motor tasks; and 9 patients showed improved reaction time. Improvement was also seen on valid tests: 8 patients improved in verbal memory; 9 patients improved in visual memory; 4 patients improved in visual motor tasks; and 2 patients improved on reaction time (Figures 1-7; Table 1).

Additionally, 22 patients scored average or above in at least one composite category during both baseline and post-injury testing. Of these 22 patients, 11 showed a deficit in at least 1 of the 4 composite categories; the remaining 11 patients scored average or above in all four categories. Patients that scored below average, or worse, in all 4 categories of the baseline study had a worse score in at least 1 category of post-injury testing.

These results indicate a substantial number of invalid or potentially invalid baseline ImPACT tests results, which makes comparison to post-injury tests unreliable or questionable at best. A first draft of the manuscript to report the results of Specific Aim #1 has been completed.

Specific Aim #2: Assess the frequency of ImPACT cognitive testing suggesting ongoing impairment while the patient continues to report or demonstrate ongoing problems based on ImPACT symptom endorsement or SCAT-2/NFLSCAT. This Aim was achieved.

Specific Aim #3: Assess the frequency of ImPACT cognitive testing suggesting ongoing impairment while the patient demonstrates no evidence of ongoing problems based on ImPACT symptom endorsement or SCAT 2/NFLSCAT. This Aim was achieved.

Specific Aim #4: Assess the frequency of ImPACT cognitive testing suggesting no impairment while the patient continues to report or demonstrate ongoing problems based on ImPACT symptom endorsement or SCAT 2/NFLSCAT. This Aim was achieved.

Specific Aims #2-4 have been separated from Specific Aim #1 and have been analyzed as a group because they address issues related to post-injury ImPACT testing and patient self-report of symptoms, and are not related to baseline ImPACT testing. Table 2 shows the raw numbers (and corresponding percentages) of all post-injury ImPACT test results (n=541; up to 5 individual reports for a given patients) presented in a Chi square format for the 4 main categories of verbal memory, visual memory, visual motor, and reaction times in the database as they segregate into cognitively intact (without or with [SA#4] symptoms) and cognitively impaired (without [SA#3] or with [SA#2] symptoms). Per ImPACT's guidelines, patients were considered cognitively intact if their composite score had a percentile rank of average or above, whereas patients were considered cognitively impaired if their composite score had a percentile rank of low average and below. Correspondingly, patients were considered asymptomatic if they scored <7 on the concussion symptom severity scale, whereas patients were considered symptomatic if they scored ≥7 on the scale. Importantly, these post-injury ImPACT data indicated that approximately 40% of all patients were categorized as cognitively intact yet symptomatic, or cognitively impaired while asymptomatic, thereby suggesting possible inaccurate diagnostic and/or patient symptom self-report data.

The above data were subdivided and further analyzed based on the first post-injury ImPACT test administered and the associated patient symptom self-report data. These data include 267 subjects (163 males, 104 females) with an age range of 10-64 years. Table 3 shows the raw numbers (and corresponding percentages) of these data. Importantly, and interestingly, these data from the first post-injury ImPACT test indicate that approximately 40% of the patients were categorized as cognitively intact yet symptomatic, or cognitively impaired while asymptomatic, strikingly similar to the data obtained when all ImPACT test data (up to 5 for individual patients) were assessed. A first draft of the manuscript to report the results of Specific Aims #2-4 is in preparation.

Statistics

Figure 1. Frequency by Age

Age	Number	Percentage
11	4	5.6
12	12	16.7
13	7	9.7
14	15	20.8
15	10	13.9
16	18	25
17	3	4.2
18	3	4.2

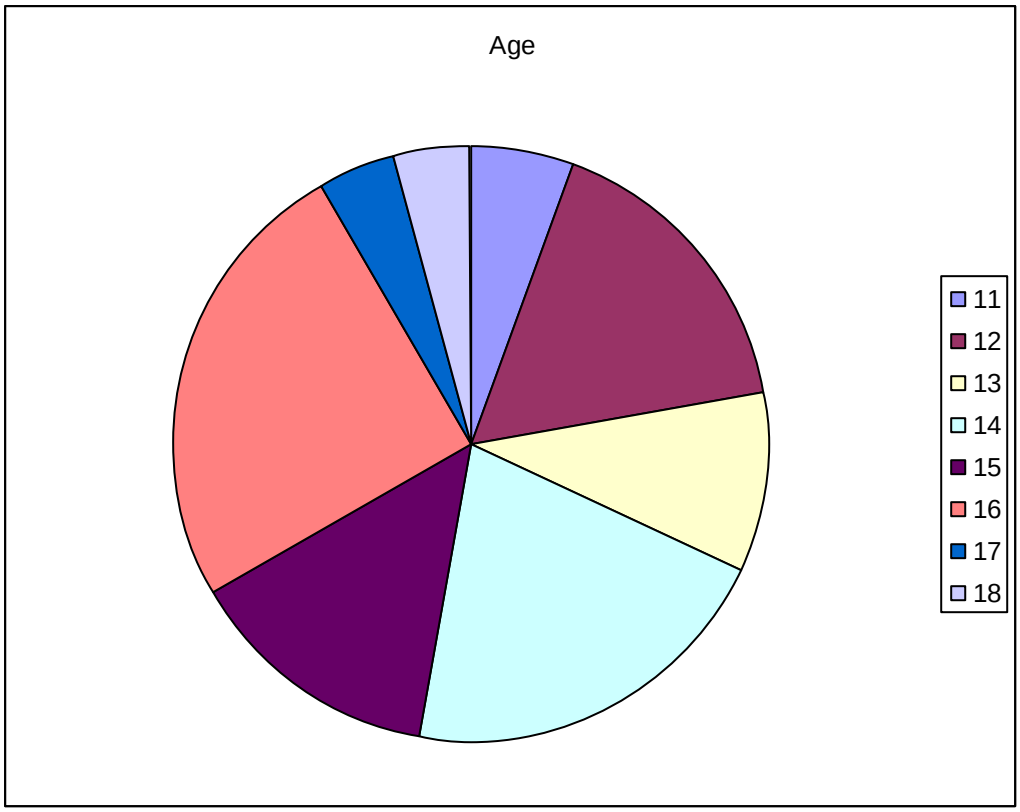
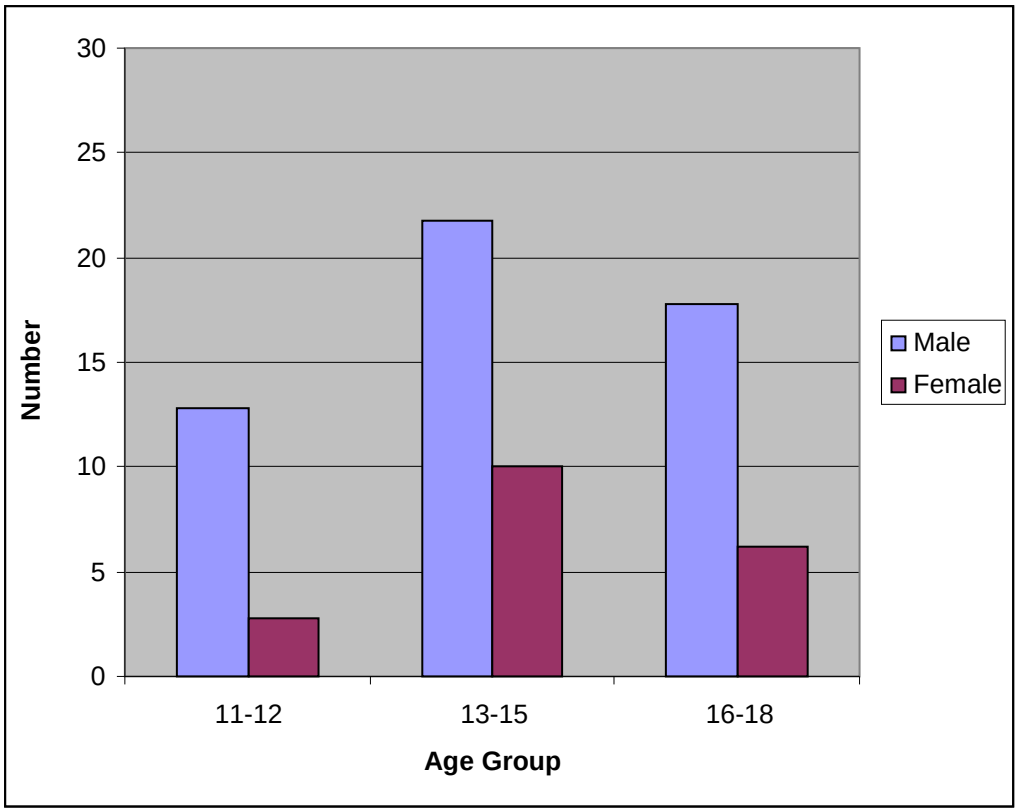


Figure 2. Segregation by Age

Age Group	Number	Percent
11-12 Male	13	13.9
13-15 Male	22	34.7
16-18 Male	18	25.0
11-12 Female	3	4.2
13-15 Female	10	13.9
16-18 Female	6	8.3



Baseline and Post-Injury Testing

Figure 3. Verbal Memory

Baseline Testing of Verbal Memory

Category	Frequency	Percentage
Impaired	1	1.4
Borderline	8	11.1
Low Average	11	15.3
Average	28	38.9
High Average	15	20.8
Superior	6	8.3
Very Superior	3	4.2

Post-Injury Testing of Verbal Memory

Category	Frequency	Percentage
Impaired	9	12.5
Borderline	16	22.2
Low Average	9	12.5
Average	17	23.6
High Average	14	19.4
Superior	5	6.9
Very Superior	2	2.8

Verbal Memory

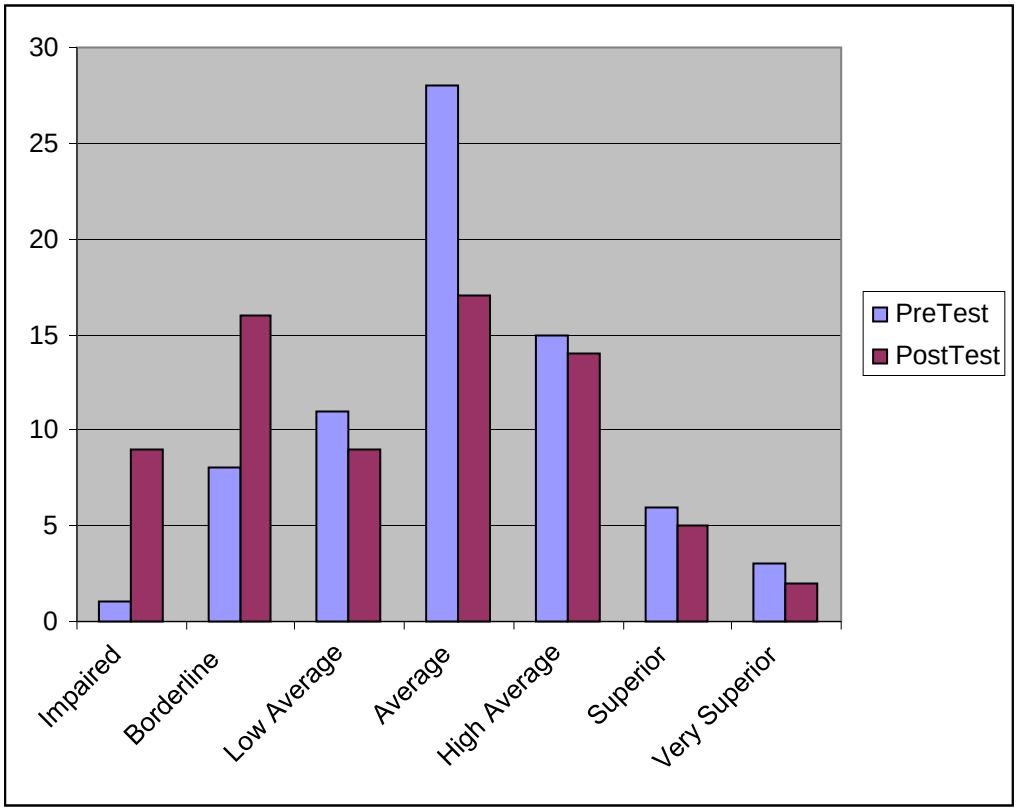


Figure 4. Visual Memory

Baseline Visual Memory

Category	Frequency	Percentage
Impaired	3	4.2
Borderline	10	13.9
Low Average	13	18.1
Average	29	40.3
High Average	11	15.3
Superior	6	8.3
Very Superior	0	0

Post-Injury Visual Memory

Category	Frequency	Percentage
Impaired	9	12.5
Borderline	17	23.6
Low Average	9	12.5
Average	24	33.3
High Average	9	12.35
Superior	3	4.2
Very Superior	1	1.4

Visual Memory

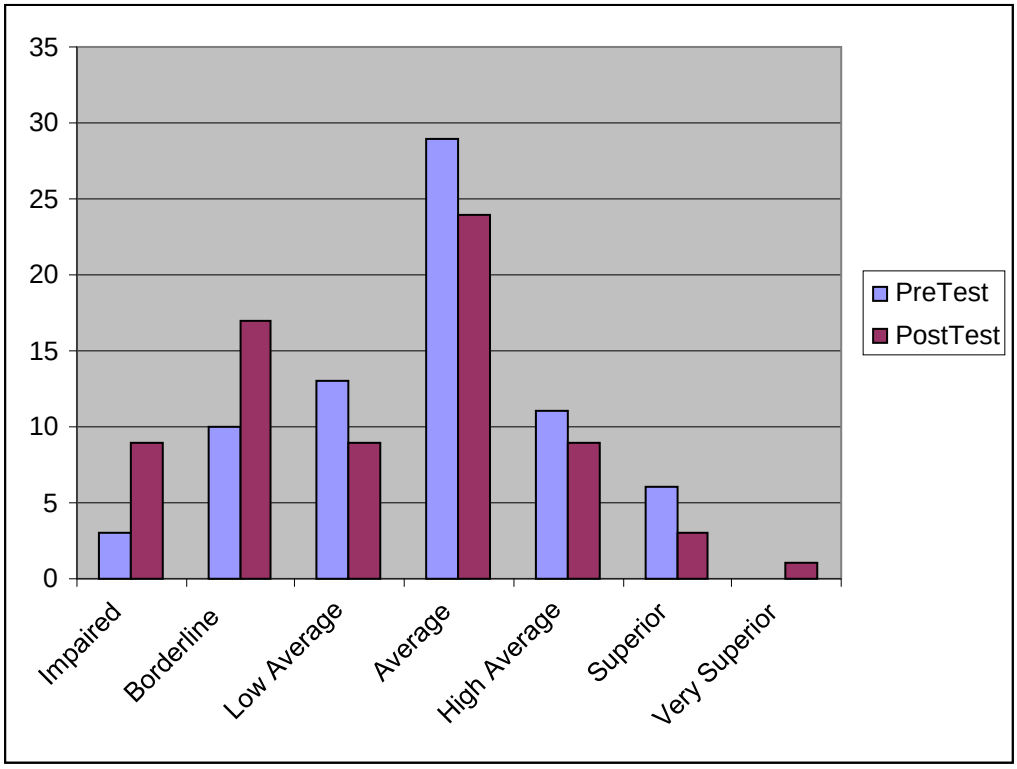


Figure 5. Visual Motor

Baseline Visual Motor

Category	Frequency	Percentage
Impaired	7	9.7
Borderline	6	8.3
Low Average	19	26.4
Average	29	40.3
High Average	5	6.9
Superior	4	5.6
Very Superior	2	2.8

Post-Injury Visual Motor

Category	Frequency	Percentage
Impaired	14	19.4
Borderline	17	23.6
Low Average	17	23.6
Average	19	26.4
High Average	4	5.6
Superior	14	1.4
Very Superior	0	0

Visual Motor

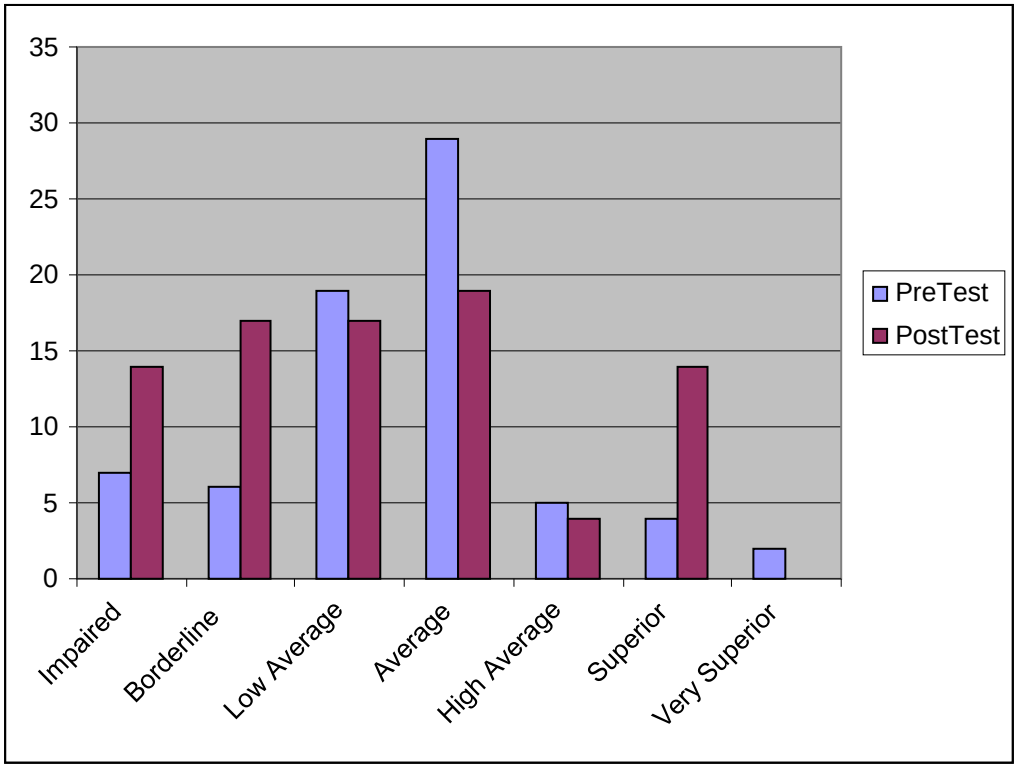


Figure 6. Reaction Time

Baseline Reaction Time

Category	Frequency	Percentage
Impaired	1	1.4
Borderline	8	11.1
Low Average	6	8.3
Average	40	55.6
High Average	12	16.7
Superior	5	6.9
Very Superior	0	0

Post-Injury Reaction Time

Category	Frequency	Percentage
Impaired	8	11.1
Borderline	17	23.6
Low Average	15	20.8
Average	25	34.7
High Average	3	4.2
Superior	3	4.2
Very Superior	1	1.4

Reaction Time

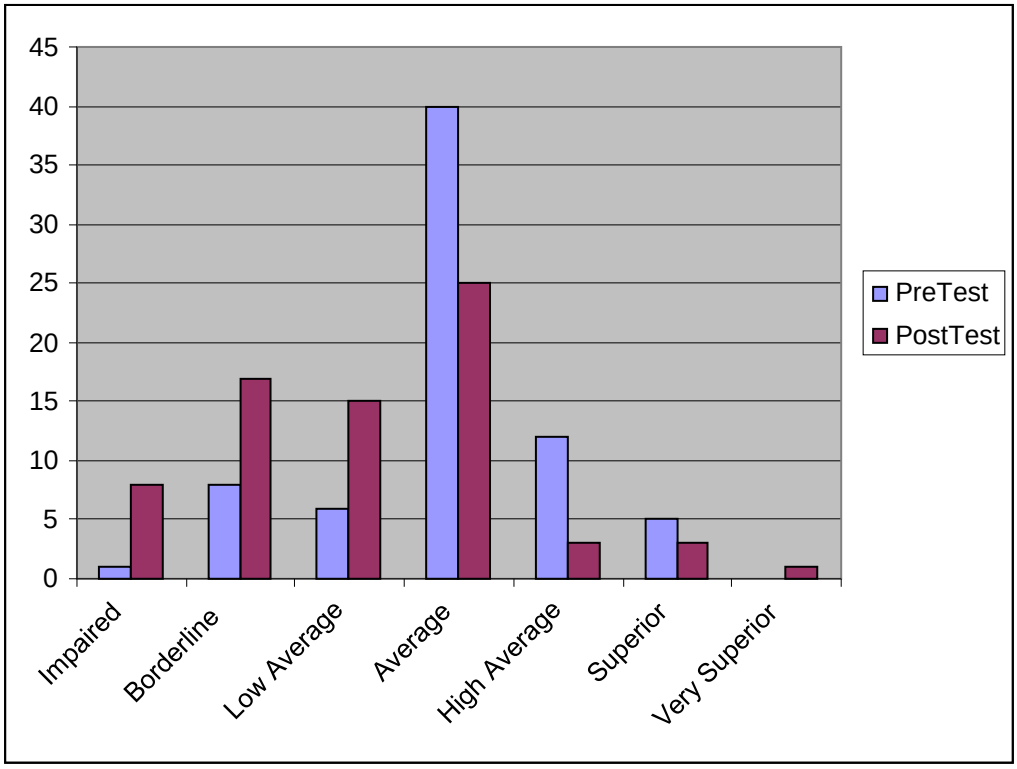


Figure 7. Improvement Post-Injury Testing

Verbal Memory

	No Improvement	Improvement
Valid	28	8
Invalid	26	10
Total	54	18

No Improvement/Worse = 75.00% Improvement = 25.00%

Visual Memory

	No Improvement	Improvement
Valid	27	9
Invalid	25	11
Total	52	20

No Improvement /Worse = 72.22% Improvement = 27.78%

Visual Motor

	No Improvement	Improvement
Valid	32	4
Invalid	29	7
Total	61	11

No Improvement/Worse = 84.72% Improvement = 15.28%

Reaction Time

	No Improvement	Improvement
Valid	34	2
Invalid	27	9
Total	61	11

No Improvement/Worse = 84.72% Improve = 15.28%

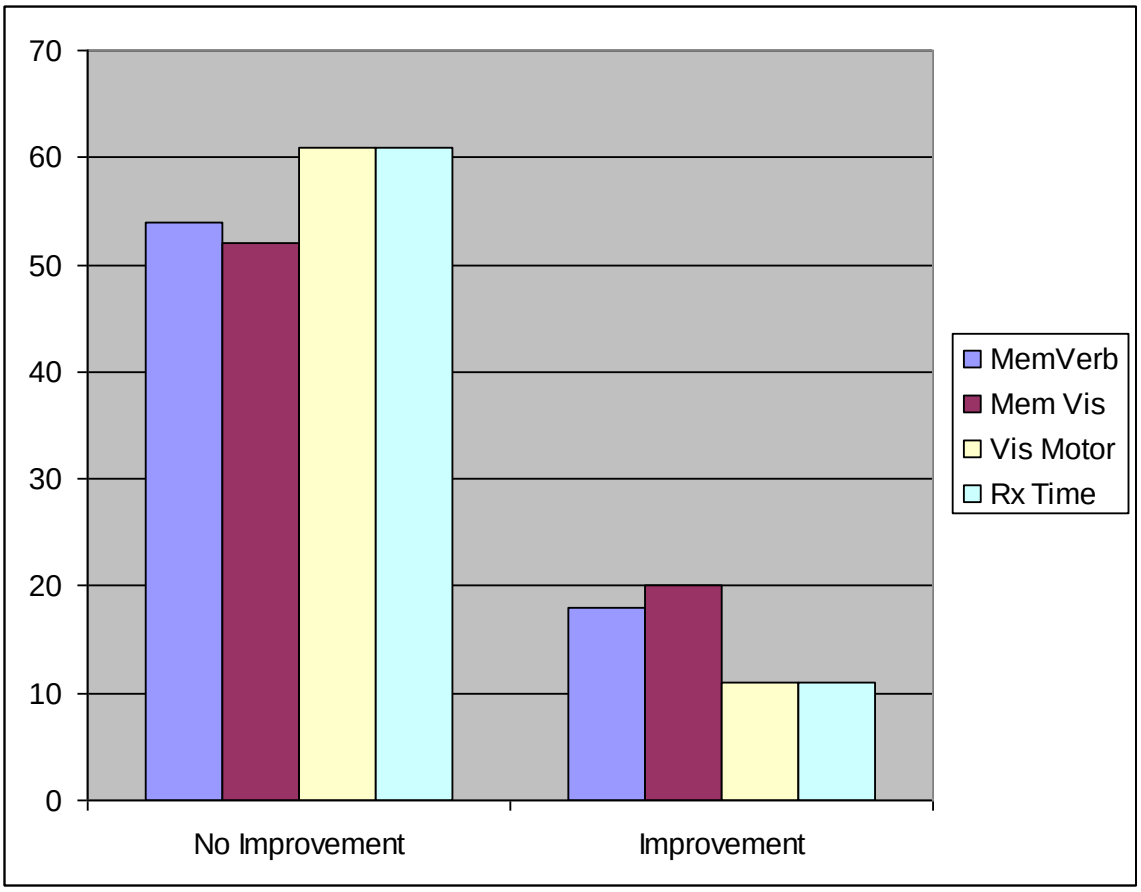


Table 1.

Improvement in classifications between baseline and post-injury testing			
Domain showing **improvement**	Baseline with no composite scores of questionable validity N=36	Baseline with at least one composite score of questionable validity N=36	Total Sample N=72
Verbal memory	8 (22%)	10 (28%)	18 (25%)
Visual memory	9 (25%)	11 (31%)	19 (23%)
Visual Motor	4 (11%)	7 (19%)	11 (15%)
Reaction Time	2 (6%)	9 (25%)	11 (15%)

Table 2. Numbers of all ImPACT post-injury tests in database (n=541)

Verbal Memory	Cog Intact	Cog Impaired
No Symptoms	183 (33.83%)	58 (10.72%)
Symptoms	159 (29.39%)	141 (26.06%)

Visual Memory	Cog Intact	Cog Impaired
No Symptoms	158 (29.21%)	83 (15.34%)
Symptoms	142 (26.25%)	158 (29.21%)

Visual Motor	Cog Intact	Cog Impaired
No Symptoms	137 (25.32%)	104 (19.22%)
Symptoms	113 (20.89%)	187 (34.57%)

Reaction Time	Cog Intact	Cog Impaired
No Symptoms	153 (28.28%)	88 (16.27%)
Symptoms	122 (22.55%)	178 (32.90%)

Table 3. Numbers of first ImPACT post-injury tests in database (n=267)

Verbal Memory	Cog Intact	Cog Impaired
No Symptoms	55 (20.60%)	19 (7.12%)
Symptoms	101 (37.83%)	92 (24.46%

Visual Memory	Cog Intact	Cog Impaired
No Symptoms	51 (19.10%)	23 (8.61%)
Symptoms	88 (32.96%)	105 (39.33%)

Visual Motor	Cog Intact	Cog Impaired
No Symptoms	39 (14.16%)	35 (13.11%)
Symptoms	68 (25.47%)	125 (46.82%)

Reaction Time	Cog Intact	Cog Impaired
No Symptoms	41 (15.36%)	33 (12.36%)
Symptoms	75 (28.09%)	118 (44.19%)

18. Extent of Clinical Activities Initiated and Completed. Items 18(A) and 18(B) should be completed for all research projects. If the project was restricted to secondary analysis of clinical data or data analysis of clinical research, then responses to 18(A) and 18(B) should be "No."

18(A) Did you initiate a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

_____Yes
___X__No

18(B) Did you complete a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

_____Yes
___X__No

If "Yes" to either 18(A) or 18(B), items 18(C) – (F) must also be completed. (Do NOT complete 18(C-F) if 18(A) and 18(B) are both "No.")

18(C) How many hospital and health care professionals were involved in the research project?

_____Number of hospital and health care professionals involved in the research project

18(D) How many subjects were included in the study compared to targeted goals?

_____Number of subjects originally targeted to be included in the study
_____Number of subjects enrolled in the study

Note: Studies that fall dramatically short on recruitment are encouraged to provide the details of their recruitment efforts in Item 17, Progress in Achieving Research Goals, Objectives and Aims. For example, the number of eligible subjects approached, the number that refused to participate and the reasons for refusal. Without this information it is difficult to discern whether eligibility criteria were too restrictive or the study simply did not appeal to subjects.

18(E) How many subjects were enrolled in the study by gender, ethnicity and race?

Gender:
_____Males
_____Females
__ ___Unknown

Ethnicity:
_____Latinos or Hispanics
_____Not Latinos or Hispanics
_____Unknown

Race:
_____American Indian or Alaska Native
_____Asian
_____Blacks or African American
_____Native Hawaiian or Other Pacific Islander
_____White
_____Other, specify:_____
_____Unknown

18(F) Where was the research study conducted? (List the county where the research study was conducted. If the treatment, prevention and diagnostic tests were offered in more than one county, list all of the counties where the research study was conducted.)

19. Human Embryonic Stem Cell Research. Item 19(A) should be completed for all research projects. If the research project involved human embryonic stem cells, items 19(B) and 19(C) must also be completed.

19(A) Did this project involve, in any capacity, human embryonic stem cells?
_____Yes
__X___No

19(B) Were these stem cell lines NIH-approved lines that were derived outside of Pennsylvania?
_____Yes
__X___No

19(C) Please describe how this project involved human embryonic stem cells:

20. Articles Submitted to Peer-Reviewed Publications.

20(A) Identify all publications that resulted from the research performed during the funding period and that have been submitted to peer-reviewed publications. Do not list journal abstracts or presentations at professional meetings; abstract and meeting presentations should be listed at the end of item 17. **Include only those publications that acknowledge the Pennsylvania Department of Health as a funding source** (as required in the grant agreement). List the title of the journal article, the authors, the name of the peer-reviewed publication, the month and year when it was submitted, and the status of publication (submitted for publication, accepted for publication or published.). Submit an electronic copy of each publication or paper submitted for publication, listed in the table, in a PDF version 5.0.5 (or greater) format, 1,200 dpi. Filenames for each publication should include the number of the research project, the last name of the PI, and an abbreviated title of the publication. For example, if you submit two publications for Smith (PI for Project 01), one publication for Zhang (PI for Project 03), and one publication for Bates (PI for Project 04), the filenames would be:

Project 01 – Smith – Three cases of isolated
Project 01 – Smith – Investigation of NEB1 deletions
Project 03 – Zhang – Molecular profiling of aromatase
Project 04 – Bates – Neonatal intensive care

If the publication is not available electronically, provide 5 paper copies of the publication.

Note: The grant agreement requires that recipients acknowledge the Pennsylvania Department of Health funding in all publications. Please ensure that all publications listed acknowledge the Department of Health funding. If a publication does not acknowledge the funding from the Commonwealth, do not list the publication.

Title of Journal Article:	Authors:	Name of Peer-reviewed Publication:	Month and Year Submitted:	Publication Status (check appropriate box below):
1.				☐Submitted ☐Accepted ☐Published
2.				☐Submitted ☐Accepted ☐Published
3.				☐Submitted ☐Accepted ☐Published

20(B) Based on this project, are you planning to submit articles to peer-reviewed publications in the future?

Yes____X_____ No_____

If yes, please describe your plans:

Two manuscripts are in preparation: The first manuscript will report the results of Specific Aim #1 – our institution's experience with the utility of baseline neurocognitive testing (ImPACT) when assessing the results of the first post-injury ImPACT testing obtained after sports-related concussion. The second manuscript will report the results of Specific Aims 2-4, which analyze post-injury ImPACT testing and are not related to baseline ImPACT testing. The focus of this manuscript is to address issues related to cognitive status, patient self-report of symptoms, and the utility of the information for informed clinical decision-making.

21. Changes in Outcome, Impact and Effectiveness Attributable to the Research Project. Describe the outcome, impact, and effectiveness of the research project by summarizing its impact on the incidence of disease, death from disease, stage of disease at time of diagnosis, or other relevant measures of outcome, impact or effectiveness of the research project. If there were no changes, insert "None"; do not use "Not applicable." Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

Important outcomes of this study include: 1) the commitment to pursue additional research in mTBI – the PI had no previous experience in clinical studies of mTBI prior to this research project; 2) expanding the exploration and development of different technologies in the diagnosis of mTBI, especially in young student athletes and soldiers; and 3), develop evidence-based guidelines for management of mTBI with integrated, best practice use of validated, state-of-the-art diagnostic tools above and beyond our current reliance on computer-based neurocognitive testing.

22. Major Discoveries, New Drugs, and New Approaches for Prevention Diagnosis and Treatment. Describe major discoveries, new drugs, and new approaches for prevention, diagnosis and treatment that are attributable to the completed research project. If there were no major discoveries, drugs or approaches, insert "None"; do not use "Not applicable." Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

As described above, the research project has provided invaluable insight to the limitations of current neurocognitive testing for the diagnosis and management of mTBI. This insight has accelerated our institution's exploration of new diagnostic approaches for mTBI, such as the NKI I-Portal oculomotor and vestibular system testing platform, as well as a newly implemented use of the *i*-COMET C3 (Comprehensive Concussion Care) program - developed at the Cleveland Clinic – for use throughout the Sports Medicine Program at AHN, which now no longer utilizes ImPACT for either baseline or post-mTBI testing of student athletes.

23. Inventions, Patents and Commercial Development Opportunities.

23(A) Were any inventions, which may be patentable or otherwise protectable under Title 35 of the United States Code, conceived or first actually reduced to practice in the performance of work under this health research grant? Yes_____ No___X_____

If "Yes" to 23(A), complete items a – g below for each invention. (Do NOT complete items a - g if 23(A) is "No.")

a. Title of Invention:

b. Name of Inventor(s):

c. Technical Description of Invention (describe nature, purpose, operation and physical, chemical, biological or electrical characteristics of the invention):

d. Was a patent filed for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes_____ No____

If yes, indicate date patent was filed:

e. Was a patent issued for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes_____ No____
If yes, indicate number of patent, title and date issued:
Patent number:
Title of patent:
Date issued:

f. Were any licenses granted for the patent obtained as a result of work performed under this health research grant? Yes_____ No____

If yes, how many licenses were granted?_____

g. Were any commercial development activities taken to develop the invention into a commercial product or service for manufacture or sale? Yes___ No____

If yes, describe the commercial development activities:

23(B) Based on the results of this project, are you planning to file for any licenses or patents, or undertake any commercial development opportunities in the future?

Yes_____ No____X_____

If yes, please describe your plans:

24. Key Investigator Qualifications. Briefly describe the education, research interests and experience and professional commitments of the Principal Investigator and all other key investigators. In place of narrative you may insert the NIH biosketch form here; however, please limit each biosketch to 1-2 pages. *For Nonformula grants only – include information for only those key investigators whose biosketches were not included in the original grant application.*

NAME	POSITION TITLE
Kevin M. Kelly	Professor of Neurology, Neurobiology and Anatomy
eRA COMMONS USER NAME (credential, e.g., agency login) kkelly	

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Saint Joseph's University, Philadelphia, PA	B.S.	1973	Biology
University of Pittsburgh, Pittsburgh, PA	M.D.	1984	Medicine
Temple University, Philadelphia, PA	Ph.D.	1987	Neurobiology
University of Michigan, Ann Arbor, MI	Fellow	1988-1990	Neuropharmacology
University of Michigan, Ann Arbor, MI	Fellow	1994-1995	EEG and Epilepsy

Graduate Training:

1974-1980 Graduate Student, Dept. of Biology, Temple U., Philadelphia, PA
1980-1984 Medical Student, School of Medicine, U. of Pittsburgh, Pittsburgh, PA
1984-1985 Intern, Internal Medicine, Dept. of Internal Medicine, The Mercy Hospital of Pittsburgh
1985-1988 Resident, Neurology, Dept. of Neurology, U. of Michigan, Ann Arbor, MI

Teaching Appointments:

1990-1991 Instructor, Dept. of Neurology, School of Medicine, U. of Michigan
1991-1994 Assistant Professor, Dept. of Neurology, School of Medicine, U. of Michigan
1995-1997 Research Scientist, Neurosciences Research Center, Allegheny U. of the Health Sciences
Attending Physician, Division of Neurology, Dept. of Internal Medicine, Allegheny General Hospital (AGH), Pittsburgh, PA
1997-2003 Associate Professor, Dept. of Neurology, College of Medicine, Drexel U., AGH, Allegheny-Singer Research Institute (ASRI)
2003- Professor, Dept. of Neurology, College of Medicine, Drexel U., AGH
2005- Director, Center for Neuroscience Research, ASRI
2009- Professor, Dept. of Neurobiology and Anatomy, College of Medicine, Drexel U., AGH, ASRI

Honors and Awards:

1988-1990 Training Grants, National Research Service Award (PI, S Gilman)
1989-1992 Research Fellowship Award, American Academy of Neurology (Mentor, RL Macdonald)
1990-1994 NINDS Clinical Investigator Development Award (K08; Mentor, RL Macdonald)
1994-1995 National EpiFellows Foundation Award (Mentor, RL Macdonald)

Memberships and Participations:

1985- Society for Neuroscience, Member
1990- American Epilepsy Society, Member

1991-	American Academy of Neurology, Active Member
2010-	American Neurological Association, Member
2001-2004	NIH Brain Disorders & Clinical Neuroscience 1 (BDCN-1) Study Section, Ad Hoc Reviewer
2003	NIH BDCN F (01) Study Section, Ad Hoc Reviewer
2003	International Geriatric Epilepsy Symposium, Steering Committee, Member
2004	American Epilepsy Society Investigators' Workshop, Moderator
2005-2008	NIH ZRG1 HOP-U-29L, Minority/Disability (Diversity) Predoctoral Fellowships Special Emphasis Panel, Ad Hoc Reviewer
2006	NIH/NINDS Workshop, Model Development in Epileptogenesis and Therapy-Resistant Epilepsy, Planning Committee, Member
2006	NIH/NINDS Workshop, Models of Geriatric Epilepsy, Planning Committee, Chair
2006	NIH/NINDS Workshop, Biomarkers of Epileptogenesis, Planning Committee, Member
2006	Citizens United for Research in Epilepsy (CURE) - Scientific Review Board, Ad Hoc Reviewer
2006-2013	Epilepsy Foundation, Grant and Fellowship Subcommittee, Ad Hoc Reviewer
2007-2009	American Epilepsy Society, Research Initiative Fund Review Committee, Member
2008	NIH Clinical Neuroscience and Disease (CND) Study Section, Ad Hoc Reviewer
2008	NIH Neurological, Aging, and Musculoskeletal Epidemiology (NAME) Study Section, Ad Hoc Reviewer
2008	NIH/NINDS Workshop, Dementia of Alzheimer's disease and Epilepsy: Converging Mechanisms, Participant
2009-2014	NIH Acute Neural Injury and Epilepsy (ANIE) Study Section, Ad Hoc Reviewer
2010-2011	NIH Exceptional, Unconventional Research Enabling Knowledge Acceleration (EUREKA) in the Epilepsies Study Section, Ad Hoc Reviewer
2011-2013	American Epilepsy Society, Investigators Workshop Committee, Member
2012-2013	NIH Special Emphasis Panel, ZRG1 BDCN-W.02, Member Conflict: Mental Disorders and Traumatic Brain Injury, Ad Hoc Reviewer

Publications

Kelly KM, Shiau DS, Jukkola PI, Miller ER, Mercadante AL, Quigley MM, Nair SP, Sackellares JC (2011) Effects of age and cortical infarction on EEG dynamic changes associated with spike wave discharges in F344 rats. Exp Neurol 232:15-21

Synowiec AS, Yandora KA, Yenugadhati V, Valeriano JP, Schramke CJ, Kelly KM (2012) The efficacy of topiramate in adult refractory status epilepticus: experience of a tertiary care center. Epilepsy Res 98:232-237

Synowiec AS, Singh DS, Yenugadhati V, Valeriano JP, Schramke CJ, Kelly KM (2013) Ketamine in the treatment of refractory status epilepticus. Epilepsy Res 105:183-188